## A. <u>INTRODUCTORY COMMENTS</u>.

Currently pending in the application are claims 1-15, 17 and 19-24. Applicants wish to thank Examiner Falk for the courtesy of an interview on June 24, 2003. During the interview, four topics were discussed. First, the Examiner's finding of nonenablement for gene therapy was discussed in light of the specification statement (page 8, lines 22-23). Second, the Examiner's previous finding of lack of functional recovery was discussed in light of the Baker article and a draft declaration by inventor McGrogan. The Examiner agreed to review a submitted declaration. Third, it was mentioned that dependent claims 2-5 were inconsistent with the amended claim 1, as claims 2-5 only recited progenitor cells; whereas, independent claim 1 recited neuronal progenitor cells. Amendment of claims 2-5 was promised. And finally, the Examiner's finding of indefiniteness of claim 24 for adding a second step a could be obviated by amendment to add a subsequent step d. This amendment contains all the points agreed to with the Examiner and an explanation of the patentability of the claimed inventions.

## B. <u>AMENDMENTS TO THE CLAIMS</u>.

- 1. (previously amended): A method of producing dopaminergic neuronal cells, said neuronal cells being derived from neuronal progenitor cells
- a. providing neuronal progenitor cells which lack at least one indicator of neuronal cell differentiation;
- b. treating the neuronal progenitor cells with an inducing agent for a time period sufficient to optimize expression of tyrosine hydroxylase and to induce the presence of at least one indicator of neuronal cell differentiation to produce a plurality of dopaminergic, differentiated neuronal cells, and
- c. minimally replating with a mitotic inhibitor to enrich for dopaminergic cells in the culture.
- 2. (amended): The method of claim 1, wherein the step of providing <u>neuronal</u> progenitor cells provides mammalian cells.
- 3. (amended): The method of claim 1, wherein the step of providing <u>neuronal</u> progenitor cells provides NT2/D1 cells.
- 4. (amended): The method of claim 1, wherein the step of providing neuronal progenitor cells provides mammalian fetal cells.
- 5. (amended): The method of claim 1 wherein the step of providing <u>neuronal</u> progenitor cells provides mammalian stem cells.
- 6. (amended): The method of claim 1, wherein step c also includes adding at least one lithium ehloride salt.
- 7. (original): The method of claim 1, wherein step c is followed by an additional step of co-culturing with at least one cell type which stabilizes or improves the dopaminergic phenotype of the cells.
- 8. (original): The method of claim 7, wherein the co-culturing step is co-culturing with human bone marrow stem cells or Sertoli cells.
- 9. (original): The method of claim 7 wherein the co-culturing step comprises co-culturing with Sertoli cells, human bone marrow stem cells, or a combination thereof.
- 10. (amended): The method of claim 1 wherein the step of treating the <u>neuronal</u> progenitor cells comprises applying retinoic acid or retinoids thereto.

- 11. (previously amended): A dopaminergic neuronal cell, said cell comprising a post-mitotic differentiated neuronal cell which expresses tyrosine hydroxylase and at least one other indicator of neuronal cell differentiation, said cell having undergone induction ex vivo from an undifferentiated neuronal progenitor cell.
- 12. (previously amended): A human post-mitotic dopaminergic cell, said cell comprising a differentiated neuronal cell which expresses tyrosine hydroxylase and at least one other indicator of neuronal cell differentiation, said cell having undergone induction ex vivo from an undifferentiated human cell.
- 13. (previously amended): A human dopaminergic cell, the cell comprising an exvivo differentiated human neuronal cell that expresses tyrosine hydroxylase and bcl-2, said cellbeing capable of synthesizing dopamine and having improved survival.
- 14. (previously amended): A method of improving the survival of human neuronal cells, said method comprising the steps of:
  - a. providing a culture of human neuronal cells; and
- b. adding a lithium salt to the human neuronal cell culture for a sufficient time to enhance expression of bcl-2.
- 15. (previously amended): A pharmaceutical dosage form of human non-fetal dopaminergic cells comprising isolated, neuronal cells, the neuronal cells being capable of expressing tyrosine hydroxylase, D2 dopamine receptor and aldehyde dehydrogenase-2, and pharmaceutical diluent.
  - 16. (cancelled).
- 17. (previously amended): The method of claim 14 wherein the lithium salt is lithium chioride
  - 18. (cancelled).
- 19. (previously amended): A method of preparing human dopaminergic neuronal cells, the method comprising
  - a. providing NT2/D1 cells;
- b. culturing NT2/D1 cells with an inducing agent fore a time sufficient to optimize tyrosine hydroxylase (TH) expression therein; and
  - c. replating and culturing the TH-optimized cells in mitotic inhibitor.

- 20. (previously amended): The method of claim 19, additionally comprising the steps of:
  - d. separating the TH-optimized cells from the replate culture;
- e. replating the TH-optimized cells on a confluent feeder cell layer, the cell layer being chosen from cells which stabilize TH production; and
- f. isolating the TH-optimized cells and stabilized cells form the replate medium.
  - 21. (previously amended): A pharmaceutical composition comprising: isolated, post-mitotic neuronal cells, the neuronal cells expressing tyrosine hydroxylase (TH), D2 dopamine receptor, and aldehyde dehydrogenase-2; cells capable of stabilizing TH production of the neuronal cells; and a pharmaceutical diluent.
- 22. (original) The composition of claim 21 in which the stabilizing cells are Sertoli cells, bone marrow stem cells or a combination thereof.
- 23. (previously added): The method of claim 20 wherein the cells which stabilize TH production comprise bone marrow stem cells, TM4 Sertoli cells, glioma cells, or a combination thereof.
  - 24. (amended): The method of claim 1 further comprising the additional step of
  - ad. harvesting the dopaminergic neuronal cells.